REMARKS

Claims 57 – 68 are pending, with claim 68 having been withdrawn from consideration pursuant to an election of species. No amendments are made herein. All prior rejections have been withdrawn in favor of new rejections of the pending claims under 35 U.S.C. § 103.

Rejections Under 35 U.S.C. § 103(a)

Claims 57 – 64 and 67 stand rejected under 35 U.S.C. § 103(a) as having been obvious over Dostert (U.S. Patent No. 5,236,957; "Dostert") and Birkmayer (U.S. Pat. No. 3,795,739; "Birkmayer") in view of Chazot (*Curr. Opin. in Investigational Drugs*, 2001; "Chazot"). Claims 65 and 66 stand rejected as unpatentable under 35 U.S.C. § 103(a) over Dostert and Birkmayer in view of Chazot, further in view of Chenard (U.S. Pat. No. 6,258,827; "Chenard"). These are the sole rejections remaining in this case. Applicants respectfully traverse.

Dostert is characterized as teaching therapy of Parkinson's disease with safinamide, (S)-2-[4-(3-fluorobenzyloxy)benzyl]aminopropionamide, or its methane sulfonate salt, in oral doses ranging from about 50 to about 1500 mg/day. The Examiner correctly notes that "Dostert does not teach the coadministration of L-DOPA . . . in an amount that alone has therapeutic effect." Final office action, page 4.

Birkmayer, a 1974 patent drawn to L-DOPA compositions and combination therapies that comprise L-tryptophan or L-5-hydroxytryptophan to reduce L-DOPA side-effects, notably psychosis, is cited for its recitation of L-DOPA compositions that further comprise peripheral decarboxylase inhibitors, such as carbidopa. Birkmayer is also cited as disclosing L-DOPA administration of 8 weeks' duration. Birkmayer makes no mention of safinamide, its salts, or its congeners.

Chenard is further cited as a tertiary reference with respect to claims 65 and 66 to document the unremarkable proposition that L-DOPA is at times administered with catechol-O-methyltransferase inhibitors, such as tolcapone or entacapone. Chenard is silent with respect to safinamide, its salts, and congeners thereof.

Chazot is applied for purposes of motivating the combination of Dostert and Birkmayer: "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to have combined safinamide, used to treat Parkinson's disease, as taught by Dostert, with a combination of L-Dopa and a peripheral decarboxylase inhibitor, as taught by Birkmayer, for the same purpose. The motivation to combine these agents is provided by Chazot. Chazot teaches the coadmin[i]stration of safinamide with that of L-Dopa in the treatment of Parkinson's disease." Final Office Action, p. 5.

In the Examiner's rejection, a reasoned assertion is not properly provided that combining Dostert with Birkmayer would have provided a reasonable expectation of successful adjunctive treatment of Parkinson's disease with safinamide, in which -- as here claimed -- L-DOPA is "administered in an amount that alone has therapeutic effect." A reasonable expectation of success is ***a required element*** of any *prima facie* case of obviousness. *In re Dow Chemical Co.*, 837 F2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) ("The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out ***and would have a reasonable likelihood of success, viewed in the light of the prior art***.") (emphasis added); *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673 (Fed. Cir. 1988); *accord, Procter & Gamble Co. v. Teva Pharmaceuticals USA Inc.*, 566 F3d 989, 90 USPQ2d 1947 (Fed. Cir. 2009); M.P.E.P. § 2143.02 (8th ed., rev. 6) ("Reasonable expectation of success ***is required***.") (emphasis added).

The PTO bears the initial burden of presenting a *prima facie* case of obviousness. When the PTO fails to meet its burden, the applicant is entitled, without more, to issuance of the patent. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002) (reversing the Board's holding of obviousness due to failure to state an adequate *prima facie* case); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992) ("If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent."); *In re Grabiak*, 226 USPQ 870, 873 (Fed. Cir. 1985) ("On the record before us, we conclude that the PTO did not establish a *prima facie* case of obviousness, and thus did not shift to Grabiak the burden of coming forward with evidence of unexpected results."). These holdings allocating procedural and substantive burdens in prosecution were left undisturbed by the Supreme Court's

subsequent decision in *KSR International Co. v. Teleflex, Inc.*, 82 USPQ2d at 1385, 1396 (2007). See *Procter & Gamble Co. v. Teva Pharmaceuticals USA Inc.*, 90 USPQ2d 1947, 566 F3d 989 (Fed. Cir. 2009). Without the ***required*** demonstration that there would have been a reasonable expectation of successfully combining the prior art disclosures to achieve applicant's claimed invention, the Examiner has failed to carry her burden. Therefore, the rejection fails, and the applicants are entitled, without more, to issuance of the claims.

However, with safinamide currently in phase III trials as an add-on to levodopa[1] and as an add-on to dopamine agonists,[2] applicants nonetheless submit the following remarks and accompanying declaratory evidence in order to expedite prosecution.

The Examiner relies on Chazot to motivate the combination of Dostert, which teaches the use of safinamide in treatment of Parkinson's disease, and Birkmayer, cited for the conjoint usage of levodopa with a peripheral decarboxylase inhibitor:

> [i]t would have been obvious to one of ordinary skill in the art at the time of the invention to have combined safinamide, used to treat Parkinson's disease, as taught by Dostert, with a combination of L-Dopa and a peripheral decarboxylase inhibitor, as taught by Birkmayer, for the same purpose. The motivation to combine these agents is provided by Chazot. Chazot teaches the coadmin[i]stration of safinamide with that of L-Dopa in the treatment of Parkinson's disease.[3]

For the reasons set forth in the accompanying Second Declaration of C. Warren Olanow under 37 C.F.R. § 1.132, Chazot "would not have motivated a person of ordinary skill ... to take *any* experimental or clinical action whatsoever in furtherance of the idea that safinamide might have benefits in PD as an 'add-on' to therapeutic doses of levodopa." Second Olanow Declaration, ¶ 10.

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1 "Safinamide in Idiopathic Parkinson's Disease (IPD) With Motor Fluctuations, as Add-on to Levodopa (SETTLE)," clinical trial identifier NCT00627640 (www.clinicaltrials.gov).

2 "MOTION, Safinamide in Early IPD, as Add-on to Dopamine Agonist," clinical trial identifier NCT00605683 (www.clinicaltrials.gov).

3 Final Office Action, p. 5.

In addition, "even if, *for sake of argument*, Chazot *were* to be credited with having motivated the adjunctive administration of safinamide with L-DOPA, none of the experiments reviewed in Chazot would have led to a reasonable expectation that the oral administration of safinamide would successfully increase the therapeutic benefit of a dose of concurrently administered L-DOPA that alone has therapeutic effect." Second Olanow Declaration, ¶ 27. The underlying reasoning is elaborated in the preceding paragraphs of the Second Olanow Declaration, at ¶¶ 11 – 26, and need not be paraphrased here.

Finally, the required expectation of success cannot be found in Birkmayer, a patent that long preceded the invention of safinamide and its congeners, nor in Chenard, which is silent with respect to safinamide, its salts, and congeners thereof. Neither is it reasonably to be found in Dostert. Although Dostert describes the use of safinamide and congeners in the treatment of Parkinson's disease – and in a divisional, U.S. Patent No. 5,502,079 (of record), Dostert indeed *claims* the use of these compounds in methods of treating Parkinson's disease – the Dostert disclosure is completely silent with respect to the subject matter here claimed, the treatment of Parkinson's disease by administration of safinamide as an adjunct to therapeutically effective doses of L-DOPA.

CONCLUSION

Claims 57 – 68 are pending, with claim 68 currently withdrawn from prosecution

The sole rejections remaining in this application, rejection of claims 57 – 67 under 35 U.S.C. § 103, have been traversed. As discussed above, the Examiner's *prima facie* case of obviousness lacks a critical element; the Examiner's characterization of Chazot as having motivated the adjunctive use of safinamide with clinically therapeutic doses of levodopa has been traversed by expert declaratory evidence; none of the cited references, and as particularly discussed in Dr. Olanow's Declaration, none of the experiments reviewed in Chazot, provides a reasonable expectation that the addition of safinamide to therapeutically effective doses of L-DOPA would provide increased therapeutic benefit. The rejections are in error, and should be withdrawn.

Rejoinder

Claim 57 is generic to the species of "Parkinson's Disease agent" previously elected for prosecution on the merits, L-DOPA. Claim 57 recites:

> A method of treating idiopathic Parkinson's disease, comprising:
> orally administering safinamide, or a pharmaceutically acceptable salt thereof, on a daily dosage schedule of about 0.5 mg/kg/day to about 2 mg/kg/day to a patient with idiopathic Parkinson's disease; and
> concurrently administering to the patient at least one Parkinson's Disease agent, wherein the at least one Parkinson's disease agent is selected from the group consisting of L-Dopa and Dopamine agonists, and wherein the at least one Parkinson's Disease agent is administered in an amount that alone has therapeutic effect.

No rejections having been predicated on the combination of safinamide with a dopamine agonist, generic claim 57 is allowable. Pursuant to 37 C.F.R. §§ 1.141 and 1.146, rejoinder and allowance of claim 68, drawn to the patentably distinct species of concurrent therapy with safinamide and Dopamine agonists, is appropriate.

Interview request

If the Examiner finds that any matters remain outstanding that preclude allowance, the Examiner is requested to contact applicants' attorney, Daniel M. Becker, at (650) 813-4874, to schedule a personal interview.

Fees

No fees beyond those required for the Request for Continued Examination, elsewhere authorized, are believed to be due in connection with this response. However, the Director is authorized to charge any additional fees that may required, or credit any overpayment, to Dechert LLP Deposit Account No. 50-2778 (**Order No.** 373987-011 US (102895)).

Respectfully submitted,

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